REMARKS

This Response is submitted in reply to the final Office Action mailed on July 6, 2009. A request for continued examination ("RCE") is submitted with this Response. The Director is authorized to charge $810.00 for the RCE and any additional fees that may be required, or to credit any overpayment to Deposit Account No. 02-1818. If such a withdrawal is made, please indicate the Attorney Docket No. 3712036.00667 on the account statement.

Claims 1-44 are pending in the application. Claims 5-16 and 22-44 were previously withdrawn from consideration. In the Office Action, Claims 1-4 and 17-21 are rejected and the Drawings are objected to. In response, the specification has been amended. These amendments do not add new matter. In view of the amendments and/or for the reasons set forth below, Applicants respectfully submit that the rejections should be withdrawn.

In the Office Action, the Drawings are objected to because Figure 18 allegedly contains nucleotide sequences that are not represented by a corresponding sequence identifier. Without acquiescing to the merits of the Examiner's objections, Applicants have submitted herewith a replacement drawing sheet for Figure 18 that contains sequence identifiers for the nucleotide sequences. Moreover, Applicants submit herewith a substitute sequence listing which contains the sequences disclosed in Figure 18 and an amendment directing it incorporation into the specification. Applicants submit that the substitute sequence listing and amendment do not introduce any new matter. Accordingly, Applicants respectfully submit that the objection to the figures be withdrawn.

In the Office Action, Claims 1-4 and 17-21 are rejected under 35 U.S.C. § 101 and 35 U.S.C. 112, first paragraph, because the claimed invention lacks patentable utility. In particular, the Office Action has alleged that the specification fails to teach a specific and substantial function for the protein set forth by SEQ ID NO: 2, as encoded by SEQ ID NO: 1, because the family of cysteine proteases is a large and variable family of enzymes. Applicants respectfully disagree with and traverse the rejection for at least the reasons set forth below.

MPEP 2107.I.A provides that "[a] 'specific utility' is specific to the subject matter claimed and can 'provide a well-defined and particular benefit to the public'." Additionally, MPEP 2107.01.I.B makes clear that to satisfy the "substantial utility" requirement, an asserted use must show that the claimed invention has a significant and presently available benefit to the public.

Applicants respectfully submit that the claimed polynucleotide (SEQ ID NO: 1) has a specific and substantial utility because it encodes a cysteine protease of SEQ ID NO: 2 (CcCP-1) that is expressed in green coffee beans where it may cleave storage proteins in the bean and thus contribute to the bean's flavor and/or aroma profile. Additionally, Applicants direct the Examiner's attention to the Declaration under 37 §1.132 of James McCarthy ("McCarthy Declaration") filed herewith. The McCarthy Declaration sets forth the results of a sequence comparison conducted between CcCP1 (the claimed polynucleotide) and CPR4, a known plant cysteine protease. The results of the sequence analysis using SignalP-NN prediction software http://www.cbs.dtu.dk/services/SignalP/ indicated that the sequence similarity between the two proteins rises to ~70% over a stretch of approximately 240 amino acids residues (see, McCarthy Declaration). Given that persons skilled in the art of molecular biology consider two proteins homologous when they exhibit greater than 35% sequence identity over a stretch of at least 100 amino acid residues, the extremely high sequence identity between CcCP1 and CPR4 indicates that they are homologous proteins which possess a similar function (See, e.g., McCarthy Declaration). As such, sufficient and credible evidence exists that the claimed polynucleotide encodes a cysteine protease. Thus, Applicants submit that a sufficient showing of utility has been made in the present specification and requests that the rejection under 35 U.S.C. § 101 and the associated rejection under § 112 be reconsidered and withdrawn.

In the Office Action, Claims 1-4 and 17-21 are rejected to under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably provide enablement for any polynucleotide encoding a polypeptide having at least 70% or 85% homology to SEQ ID NO: 2 or any polynucleotide comprising SEQ ID NO: 1 or comprising a sequence encoding SEQ ID NO: 2, wherein the polynucleotide encodes a cysteine protease. In particular, the Office Action asserts that the specification does not establish regions of the protein structure which may be modified without affecting the desired activity, the general tolerance of the desired activity to modification, a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function and the specification provides insufficient guidance as to which of the infinite possible choices are likely to be successful. Applicants respectfully traverse this rejection for at least the reasons set forth below.

The inquiry with respect to scope of enablement under 35 U.S.C. §112, first paragraph, is whether it would require undue experimentation to make and use the claimed invention. As

discussed in detail below, a consideration of all of the factors enumerated in In re Wands demonstrates that the application, in conjunction with what was known to one of skill in the art as well as other factors, teaches how to make and use the full scope of the claimed subject matter. In the BPAI precedential decision *Ex parte Kubin, reversing* the Examiner on a finding of lack of enablement with respect to appealed claims directed to an isolated nucleic acid encoding a polypeptide at least 80% identical to the amino acids set forth in SEQ ID NO:2 (a large protein of 365 amino acids), where the polypeptide binds CD48, the Examiner stated that while:

> ...molecular biology is generally an unpredictable art (and thus was so at the time the application was filed)... the other Wands factors weigh in Appellants' favor, particularly "the state of the art" and "the relative skill of those in the art," *In re Wands*, 858 F.2d 731, 736, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), as evidenced by the prior art teachings and Appellant's Specification. The amount of experimentation to practice the full scope of the claimed invention might have been extensive, but it would have been routine. The techniques necessary to do so were well known to those skilled in the art. *Ex Parte Marek Z. Kubin and Raymond G. Goodwin* Appeal No. 2007-0819 (BPAI 2007).

As discussed in detail below, in this instance the state and knowledge of skill in the art, the relative skill in the art far exceeds any alleged unpredictability of the full scope of the claimed subject matter.

Applicants respectfully submit that polynucleotides encoding polypeptides with at least 70% or 85% homology to SEQ ID NO: 2 are enabled by the instant specification. Conventional methods of molecular biology and recombinant DNA techniques were known to one of skill of the art as of the effective filing date of the instant application. Such techniques are described in numerous books and other references, see, e.g., Sambrook, *et al.* Molecular Cloning: A Laboratory Manual (2nd Edition, 1989); Maniatis *et al.* Molecular Cloning: A Laboratory Manual (1982); DNA Cloning: A Practical Approach, vol. I & II (D. Glover, ed.); Oligonucleotide Synthesis (N. Gait, ed., 1984); Nucleic Acid Hybridization (B. Hames & S. Higgins, eds., 1985); Transcription and Translation (B. Hames & S. Higgins, eds., 1984); Animal Cell Culture (R. Freshney, ed., 1986); Perbal, A Practical Guide to Molecular Cloning (1984).

Also, at the time of filing the application, molecular biology techniques to effect mutations of a polypeptide sequence were routine. Examples of such well known techniques can be found in Molecular Cloning: A Laboratory Manual 2nd Edition, Sambrook *et al*, Cold Spring Harbor, N.Y. (1989). Examples of conventional molecular biology techniques include, but are

not limited to, in vitro ligation, restriction endonuclease digestion, PCR, site-directed mutagenesis, saturation mutagenesis, cellular transformation, hybridization, electrophoresis, DNA sequencing, all of which can be used to practice the subject matter as claimed to generate domain-exchanged binding molecules.

Moreover, it respectfully is submitted that variants within the scope of the claim can be readily produced, and thus it would not be unpredictable to generate protein variants within the scope of the claims and test each for cysteine protease activity. It is known in the field of molecular biology that only a few amino acid residues are invariant within a protein sequence, while the other residues are variant and can be changed without substantial effects on protein activity (see e.g. James U. Bowie *et al.*, Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions, 147 Science 1306 (1990)). Thus, combined with the knowledge of the domains and amino acids required for activity of the claimed cysteine protease, it would be routine for one of skill in the art to predictably generate variants within the scope of the claims. Thus, it is respectfully submitted that using routine molecular biology techniques, one skilled in the art will identify numerous residues through the protein that can be changed and still retain cysteine proteinase activity. Consequently, one having ordinary skill in the art would be able to practice Claims 1-4 and 17-21 without undue experimentation. Based on at least these noted reasons, Applicants believe that Claims 1-4 and 17-21 fully comply with the enablement requirement of 35 U.S.C. §112, first paragraph. Accordingly, Applicants respectfully request that the rejection of Claims 1-4 and 17-21 under 35 U.S.C. §112 be withdrawn.

In the Office Action, Claims 1-4 and 17-21 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. In particular, the Office Action alleges that the instant specification fails to teach the claimed genus of polynucleotides encoding proteins with cysteine protease activity. Applicants respectfully traverse this rejection for at least the reasons set forth below.

An adequate written description of a claimed genus need provide "relevant, identifying characteristics" sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention (MPEP §2163). The Enzo court, citing the Guidelines, stated that "the written description

requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics...complete or partial structure, other physical chemical properties, *functional characteristics when coupled with a known or disclosed correlation between function and structure*, or some combination of such characteristics.'" *Enzo Biochem, Inc. v. Gen-Probe, Inc.* (323 F.3d 956, 964 (Fed. Cir. 2002) (emphasis in original). Further, the Guidelines set forth that a relevant identifying characteristic can be stated in terms of a function. For example, the Guidelines state as follows:

> For example, if the art has established a strong correlation between structure and function, one skilled in the art would be able to predict with a reasonable degree of confidence the structure of the claimed invention from a recitation of its function. Thus, the written description requirement may be satisfied through disclosure of a function and minimal structure when there is a well-established correlation between structure and function. MPEP §2163.

In the instant application, Applicants respectfully submit that the claimed polypeptides are sufficiently described based on identifying characteristics shared among the genus of claimed polypeptides, *i.e.* the feature of having a cysteine protease active site, which correlates the structure of the claimed polypeptides with their function as a cysteine protease. Notably, the instant claimed are drawn to a polynucleotide encoding a polypeptide with cysteine protease activity. As such, the potential genus is not as large as asserted by the Examiner. Moreover, the disclosed nucleotide specie encodes a cysteine protease with a conserved cysteine protease active site. It would be clear to one of skill in the art how to modify the disclosed polynucleotide specie (SEQ ID NO: 1) to arrive at a cysteine protease as represented by SEQ ID NO: 2. Such modification to the disclosed polynucleotide specie can be purposefully made to retain the active site of the cysteine protease. Accordingly, Applicants respectfully submit that the rejection of Claims 1-4 and 17-21 be withdrawn.

For the foregoing reasons, Applicants respectfully request reconsideration of the above-identified patent application and earnestly solicit an early allowance of same.

The Commissioner is hereby authorized to charge deposit account 02-1818 for any fees which are due and owing.

Respectfully submitted,

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